

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
28 April 2005 (28.04.2005)

PCT

(10) International Publication Number  
**WO 2005/037196 A2**

(51) International Patent Classification<sup>7</sup>: **A61K**

(21) International Application Number:  
PCT/US2004/032570

(22) International Filing Date: 5 October 2004 (05.10.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/508,290 6 October 2003 (06.10.2003) US

PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,  
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,  
ZW.

(84) Designated States (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Declarations under Rule 4.17:**

- *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)*
- *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations*
- *of inventorship (Rule 4.17(iv)) for US only*

**Published:**

- *without international search report and to be republished upon receipt of that report*

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

(71) Applicant (*for all designated States except US*): CYTOVIA, INC. [US/US]; 6650 Nancy Ridge Drive, San Diego, California 92121 (US).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): CAI, Sui Xiong [US/US]; 3623 Berryfield Court, San Diego, California 92130 (US). PERVIN, Azra [PK/US]; 41101 Arron Court, Murrieta, California 92562 (US). KASIBHATLA, Shailaja [US/US]; 13073 Dressage Lane, San Diego, California 92130 (US). NGUYEN, Bao Ngoc [US/US]; 11695 Westview Parkway, San Diego, California 92126 (US).

(74) Agents: ESMOND, Robert, W. et al.; Sterne, Kessler, Goldstein & Fox P.L.L.C., 1100 New York Avenue, N.W., Washington, DC 20005 (US).

(81) Designated States (*unless otherwise indicated, for every kind of national protection available*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,

(54) Title: SUBSTITUTED 2-ARYLMETHYLENE-N-ARYL-N'-ARYL-MALONAMIDES AND ANALOGS AS ACTIVATORS OF CASPASES AND INDUCERS OF APOPTOSIS

(57) Abstract: The present invention is directed to substituted 2-arylmethylene-N-aryl-N'-aryl-malonamides and analogs thereof. The present invention also relates to the discovery that the compounds are activators of caspases and inducers of apoptosis. Therefore, the activators of caspases and inducers of apoptosis of this invention can be used to induce cell death in a variety of clinical conditions in which uncontrolled growth and spread of anormal cells occurs.

WO 2005/037196 A2